

wherein SDTBM is a state-dependent tissue binding moiety that comprises one or more alkyl, cycloalkyl, aryl, or heterocyclic groups or combinations thereof,

the contrast agent further having:

- 1) an R1 observed value in a 4.5 wt% solution of HSA at 25 °C of greater than about  $10 \text{ mM}^{-1} \text{ sec}^{-1}$ ; and
- 2) a percent binding to HSA in a 4.5 wt%, pH 7.4 solution of HSA of greater than about 10%;

- b) subjecting the patient to magnetic resonance imaging to determine an initial signal intensity value in a region of interest of the undesired tissue;
- c) applying an interventional therapy to at least a portion of the tissue in order to treat the tissue, the interventional therapy selected from the group consisting of a thermal energy generation, a cryoablation, an injection of a denaturing liquid, an injection of a chemotherapeutic agent, and a photodynamic therapy;
- d) contemporaneously monitoring with magnetic resonance imaging a change in the initial signal intensity value in the region of interest of the undesired tissue during the interventional therapy; and
- e) stopping the interventional therapy application when the change in the initial signal intensity value in the region of interest of the undesired tissue is more than about a 50% reduction in the initial signal intensity value.

65. (new) The method of claim 64, wherein the paramagnetic metal ion complexed to the metal chelate is selected from the group consisting of Gd(III), Fe(III), Mn(II), Mn(III), Cr(III), Cu(II), Dy(III), Ho(III), Er(III), Pr(III), Eu(II), Eu(III), Tb(III), and Tb(IV), and wherein the metal chelate comprises an organic chelating agent.

66. (new) The method of claim 65, wherein the organic chelating agent is selected from the group consisting of DTPA, DOTA, HP-DO3A, and DTPA-BMA.

67. (new) The method of claim 66, wherein the organic chelating agent comprises DTPA and wherein the paramagnetic metal ion complexed to the metal chelate is Gd(III).

68. (new) The method of claim 67, wherein the organic chelating agent comprising DTPA is covalently bound to the linker L at an acetate chelating moiety of the DTPA.

69. (new) The method of claim 68, wherein the organic chelating agent comprising DTPA is covalently bound to the linker L at a methylene carbon of the acetate chelating moiety of the DTPA.

70. (new) The method of claim 67, wherein the organic chelating agent comprising DTPA is covalently bound to the linker L at an ethylene carbon backbone moiety of the DTPA.

71. (new) The method of claim 66, wherein the SDTBM comprises two or more cycloalkyl or aryl groups or combinations thereof and wherein the two or more cycloalkyl or aryl groups or combinations thereof are arranged in a rigid, non-planar orientation.

72. (new) The method of claim 71, wherein at least one of the two or more cycloalkyl or aryl groups is a cyclohexyl group.

73. (new) The method of claim 64, wherein the  $R_{\text{observed}}$  value is greater than about  $20 \text{ mM}^{-1} \text{ sec}^{-1}$ .

74. (new) The method of claim 73, wherein the  $R_{\text{observed}}$  value is greater than about  $30 \text{ mM}^{-1} \text{ sec}^{-1}$ .

75. (new) The method of claim 74, wherein the  $R_{\text{observed}}$  value is greater than about  $40 \text{ mM}^{-1} \text{ sec}^{-1}$ .

76. (new) The method of claim 64, wherein the percent binding to HSA is greater than about 50%.

77. (new) The method of claim 76, wherein the percent binding to HSA is greater than about 80%.

78. (new) The method of claim 77, wherein the percent binding to HSA is greater than about 95%.

79. (new) The method of claim 64, wherein the tissue is selected from the group consisting of cancerous tissue, tumorous tissue, and neoplastic tissue.

80. (new) The method of claim 79, wherein the tissue is cancerous tissue.

81. (new) The method of claim 64, wherein the interventional therapy application is the generation of thermal energy, and wherein the thermal energy is generated by a source selected from the group consisting of one or more focused ultrasound waves, radiofrequency waves, microwaves, and lasers.

82. (new) The method of claim 64, wherein the physiologically compatible linker L is selected from the group consisting of linear alkyl, branched alkyl, cyclic alkyl, aryl, ether, polyhydroxyl, polyether, polyamine, heterocyclic, peptide, peptoid, phosphodiester, and amide moieties.

83. (new) The method of claim 64, wherein the contrast agent is selected from the group consisting of MS-315, MS-317, MS-322, MS-323, MS-325, MS-326, MS-327, and MS-328. --

#### REMARKS

Applicants acknowledge with appreciation receipt of the "Decision Granting Petition and Assignment of Application Number and Notice of Omitted Items," dated Mar. 4, 2002 ( in Parent Application No. 08/942,989), and the "Notice of Incomplete Nonprovisional Application," dated